

Osteoarthritis (OA): A Modern Disease of the Anthropocene Era

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Abstract

In this paper we discuss recent studies that have unravelled important roles for modern-day environmental factors in the pathogenesis of osteoarthritis (OA). OA is a relatively modern disease in terms of human evolution. While our ancestors have been around for about six million years, modern humans (*Homo sapiens*) only evolved about 200,000 years ago. Early humans did not live long enough to suffer from age-related musculoskeletal conditions such as OA and arthritic diseases are thought to have been extremely rare in early Natufians and Egyptians, but this is probably because of an underrepresentation of older adults in the skeletal records. Examination of Egyptian skeletal records from burial sites provides some evidence of arthritic diseases such as OA, but mainly in the mummified remains of pharaohs and high-ranking officials, viziers, priests and nobles. Examination of the skeletal records in Roman burial ground does reveal more evidence of arthritic diseases but the evidence is sketchy and we can only assume that arthritic diseases were more prevalent in the slave population in ancient Egypt and the Roman Empire. Recent studies indicate that independent risk factors for knee OA either arose or have become amplified in the post-industrial era, suggesting that the prevalence of OA has gradually increased since the industrial revolution. Alarmingly, the incidence of knee OA has doubled since the middle of the 20th century, suggesting that OA is a modern disease of the Anthropocene era and there may be unknown environmental factors that have led to its increased incidence since industrialization.

Commentary

A recently published paper by Francis Berenbaum, Ian J. Wallace, Daniel E. Lieberman and David T. Felson in *Nature Review Rheumatology* entitled: "Modern-day environmental factors in the pathogenesis of osteoarthritis" has challenged our understanding of the pathogenesis of osteoarthritis (OA). In this original and timely article the authors propose the possibility that osteoarthritis (OA) is an evolutionary mismatch disease¹. They argue that OA is much more common today than in the past because deleterious genes inherited from previous generations may be inadequately or imperfectly adapted to our modern environment. They also identify four major contributing environmental factors including obesity, metabolic syndrome, dietary changes and physical inactivity and propose that since these have become so ubiquitous, they are accelerating the process of OA pathogenesis, especially within the past half-century. These arguments extend ideas proposed in another elegant study published in *PNAS* in 2017 by Wallace and co-workers suggesting that since the mid-20th century OA has doubled in prevalence and independent risk factors for knee OA either arose or have become amplified in the post-industrial era².

We would like to extend the ideas put forward by Berenbaum and colleagues¹ and Wallace and co-workers² and propose that OA is a modern disease of the "Anthropocene Era", an epoch dating from the commencement of significant human impact on the Earth's geology and ecosystems. In addition to the factors cited by Berenbaum and colleagues, it also appears that OA is also associated with ageing, poor diets and heavy labor³. The world's increased average age and decreased death rates, mean that people

are now living longer and are increasingly susceptible to non-communicable diseases, including cancer, cardiovascular disease, chronic respiratory diseases, diabetes, metabolic diseases and musculoskeletal (MSK) disorders including OA⁴. There is an association between OA and other chronic diseases.

OA is a modern disease in terms of human evolution and is closely linked to the beginning of the "Anthropocene". The Anthropocene is defined by global environmental changes introduced by humans. These environmental changes include rapid climate and environmental changes brought about by anthropogenic activity. Although early Homo sapiens were most likely responsible for the extinction of large mammals, particularly in North America, they otherwise had little impact on the natural environment. In contrast, modern humans have had the most destructive global impact on other species and the climate in recent geological time ⁷. Although civilization as we know it is only about 6,000-8,000 years old, the major changes in our environment began with industrialization in the 1800s. Therefore, most of the significant impact on the planet mediated by humans occurred over the last 200 years.

So, what is the relevance of human evolution and industrialisation to joint disease, and especially to OA? Berenbaum and colleagues propose that OA is an "evolutionary mismatch disease" in which modern-day factors are crucially important ¹. There is compelling evidence from epidemiological research and the WHO that the industrial revolution caused a sharp rise in the incidence of inflammatory diseases such as cancer, obesity and arthritis. The increased dependency of humans on mechanised vehicles, the significantly reduced levels of physical activity associated with urbanisation, and the consumption of obesogenic processed foods (i.e. foods high in sugar and saturated fat and low in fibre) have been proposed to be key components of the modern environment that is believed to drive the development of obesity ⁸ and the sedentary activities and behaviour changes associated with becoming overweight and obese. These behavioural changes appear to be essential pre-requisites for the pathogenesis and progression of OA ⁹.

However, skeletal records suggest that obesogenic diets and lack of activity were not the only reasons for an increase in OA in modern humans. Archaeologists examining skeletal records found that arthritis was extremely rare in early human settlements, including the Natufians, who were Epi-Paleolithic hunter-gatherers living in the Levant region of the near east between about 12,500 and 10,200 years ago. This could be because of an underrepresentation of older adults in the Natufian skeletal records. The most convincing evidence for arthritis among Natufian skeletal remains, suggests that high functional demands, with evidence of wear and tear in hands, hips and knees, among female Natufian homemakers was responsible for the development of OA. Among the Natufians, OA was associated with settlement in one place in villages, with domesticated animals and the planting of crops that we recognise as wheat and barley today.

OA and other arthritic diseases were rare in early Egyptian civilisation. The skeletal records only provide evidence of OA in mummified remains of the highest ranking members of ancient Egypt including pharaohs, viziers, high priests and nobles who had a much greater life expectancy than the rest of the population ¹⁰. There is also data from archaeological digs of Native American ¹¹⁻¹³ settlements that

suggests that a combination of major alterations in diet (i.e. relying more on carbohydrates derived from agriculture and less on hunting and gathering) and increased workload predisposed to the development of arthritis.

Therefore, it would seem plausible to suggest that a sedentary lifestyle predisposes to the development of obesity, and this leads to metabolic disease which in turn accelerates the development of OA in modern sedentary humans. However, there is also evidence from the skeletal records that suggests that a poor diet coupled with heavy workloads leads to OA, likely through alternative biomechanical mechanisms. Equally, there is evidence of OA and other forms of arthritis in Roman slaves, suggesting that lifestyle was a major contributor to the development of these diseases.

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